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ON CERTAIN EFFECTS

OF

STARVATION ON VEGETABLE AND ANIMAL TISSUES.

BY

D. D. CUNNINGHAM, M.B.,

SPECIAL ASSISTANT TO THE SANITARY COMMISSIONER WITH THE GOVERNMENT OF INDIA.

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Connection of fatty degeneration with insufficient nutritive supply a recognised fact in pathology.

That insufficient supply of nutritive material is closely connected with fatty degeneration of tissue is a well-ascertained pathological phenomenon. Rindfleisch, in his work on Pathological Histology, expresses himself as follows in regard to this subject: "This (the exclusively pathological category of fatty metamorphosis) includes all cases of disproportion between the means of nutrition and the parenchyma to be nourished. Such a disproportion may be caused either by a diminution of the *nutriens*, or by an increase of the *nutriendum*. If a minute vessel in the brain is plugged, the circulation in the area which it supplies is not wholly suspended, owing to the manifold anastomoses with neighbouring vessels; nevertheless, a very considerable retardation of the current takes place, which may even give rise to temporary stasis and to hæmorrhage, and this suffices to disturb nutrition, and so to cause fatty metamorphosis."[1]

Examples of such connection.

It is easy to find other concrete instances of fatty degeneration in association with impaired supply of nutritive material. The fatty degenerations of various tissues occurring in old age, in disused organs, and in tissues and organs where increase in bulk has been disproportionate to vascular supply, are currently cited as examples of it.

Fatty degeneration not generally recognised as an effect of starvation.

While this is the case, however, it is by no means generally recognised that fatty degeneration of tissue is an accompaniment of the general deprivation of nutritive supply incident on starvation. On the contrary we find such a distinguished authority as Bauer writing as follows:—" During a period of thirty days of starvation the body loses the greater part of its organic albumen (*Organeiweiss*) without the cells becoming incapable of performing their functions; they continue to act and are capable of full recovery on the addition of material, and death results when the actions produced by the decompositions are no longer sufficient to permit of vital phenomena. There is here a gradual emaciation or atrophy of the organic albumen, but no breaking down o cells into detritus."[1]

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[1] Manual of Pathological Histology, by Dr. Eduard Rindfleisch, (English translation,) vol. i, p. 29.

Consequent necessity of experimental investigation.

Although practical experience in regard to the effects of insuffi nourishment on the population of famine-stri areas, as well as many phenomena in the orga those dying of diseases incident on starvation, rendered the accuracy of conclusions very questionable, it yet appeared necessary to investigate the su experimentally, more especially as the interpretation of the phenomena sented by the tissues of subjects of famine dying of special diseases, su diarrhœa and dysentery, is beset with certain fallacies dependent partly o presence of the diseased conditions themselves as distinct from non-compli starvation, and partly on the remedial treatment which may have employed. The results of experimental enquiry into the subject occup earlier sections of this report as an introduction to the details regardin phenomena observed in the human subject.

Tissues of higher forms of animal and vegetable life composed both of living and formed materials.

In regard to all the higher forms of life, whether animal or vegetable, now generally recognised that they are composed of living material, and of v structures developed from and by this material, but that these structures, retaining more or less distinct structural evidence of their genetic relati living material, cannot be regarded as them alive. Such are the walls of cell-cavities tubular or filamentous structures, &c., in animal and vegetable tissues. are, no doubt, in many cases dependent for their integrity on the prese the living material connected with them, but in others they may persi various periods practically unchanged after the disappearance of the material, and in any case they have entirely ceased to exhibit any o essential characteristics of living matter. They are never developed e under the influence of living material, but the latter can be developed inde ent of them, and can even persist and thrive for indefinite periods en apart from any of them. Changes occurring in such structures as the res insufficient supply of nutritive material can only be induced mediately through the direct influence of such deficiency on the living matter.

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[1] Der Stoffumsatz bei der Phosphorvergiftung," Von Dr. Jos. Bauer. Zeitschrift für Biologie, B S. 63—85.

primary object of the experiments in the present instance was, therefore, the determination of the effects of insufficient nutritive supply on the living material, or, in other words, on the protoplasmic constituents of the tissues.

Essential uniformity in the living materials of animals and plants.

Professor Huxley long ago defined protoplasm as "the physical basis of life" and insisted on its general uniformity in character in whatever group of living beings it may be studied," at the same time affirming that "it thus becomes evident that all living powers are cognate, and that all living forms are fundamentally of one character."[1] It cannot be supposed that any difference of opinion should exist on this point, and, such being the case, it must be evident to all that the effects produced on vegetable protoplasm by insufficient nutrition are of a nature analogous to those occurring under similar conditions in the protoplasm of animal tissues, and that the study of the former may afford much information in regard to the latter. Taking this into consideration, the reason that a series of experiments should have first been carried out on the influence of starvation on vegetable protoplasm becomes manifest.

Principles determining the selection of subjects for experiment. Nature of the vegetable organisms chosen.

In selecting particular vegetable organisms as the subject of experiment, the primary desiderata appeared to be, *1st*, to employ such as were capable of easy and accurate observation under the various conditions to which they were to be subjected; and, *2nd*, to employ such as were familiar to the observer so as to secure the best opportunities of fairly estimating the actual influence of various alterations in these conditions. Two species of mucorine fungi were accordingly selected. Both of these had been special objects of study for some years, and both are readily susceptible of artificial culture under conditions extremely favourable to accurate observation. An additional recommendation of these organisms as subjects of experiment lay in the fact that, due to their fungal nature, the processes of nutrition in them shew a more accurate correspondence to those in most animals than they do in vegetable tissues containing chlorophyll.

Forms of animal life subjected to experiment.

In regard to animal tissues the great point appeared to be to secure such as could be submitted to observation during the life of the organism to which they belonged, or in any cases under circumstances involving the smallest possible amount of manipulative interference. In order to meet these requirements, the animals selected as subjects of experiment were tadpoles. From the extreme transparency of the tissues in certain parts of these organisms, and the ease with which large numbers of them may be procured and kept under observation, they afford exceptional facilities for the conduct of experiments; and although it may not be permissible to deduce exact conclusions on all points from the phenomena observed in cold-blooded animals regarding those which will present themselves in higher forms under similar conditions, yet in so far as the general effects of defective supply of nutritive material on the living elements of the tissues are concerned, there is good reason to suppose that the phenomena in both cases must be much alike.

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[1] "On the Physical Basis of Life," Lay Sermons, Addresses and Reviews, by T. H. Huxley, LL.D., F.R.S., pp. 120—146.

Nature of experimental procedure.

In regard to both animals and vegetables the procedure employed in carrying out the experiments was similar, consisting in retaining them for various periods in fluids in which nutritive material was present in various amounts, or almost entirely absent the latter condition being secured by employing distilled water as a medium With these preliminary observations a detailed account of the results of experiment may be entered upon.

CHAPTER I.

EXPERIMENTS ON THE EFFECTS OF DEFICIENT SUPPLY OF NUTRITIVE MATERIAL ON VEGETABLE TISSUES.

Mucorine fungi employed as subjects for starvation.

THE plants subjected to experiment were, as before mentioned, both members of the mucorine order of fungi; one of them being the sole known representative of the genus *Choanephora*, the other the well-known *Pilobolus crystallinus*. Both of these fungi are of constant occurrence in the neighbourhood of Calcutta, and both are readily susceptible of cultivation in media so liquid as to allow of the easy removal of germinating conidia and spores, or portions of mycelium and fructification with a minimum of disturbance or injury. This is naturally a matter of moment when it becomes necessary to submit such structures to minute examination, or to transfer them to new media. In so far as Choanephora, however, is concerned, the nutritive fluid itself, a strong decoction of the corollæ of Hibiscus, is such as to allow of continuous observation of all the stages of growth in the fungal structures while still in it, and of ready dilution with, or entire substitution by distilled water without any disturbance of the mycelium.

The structure and life history of Choanephora.

The conidia of Choanephora when introduced into the nutritive fluid germinate almost immediately, and under ordinary circumstances produce an abundant crop of conidial fructification within twenty-four hours. Immature conidia are full of a coarsely granular oily protoplasm, but they clear up greatly as they ripen, and ultimately the oily matter is only represented by aggregations of yellowish granules, one of which is generally situated toward either extremity of each oval conidium. When the conidia are subjected to conditions permitting of their germination, the first change which occurs in them is a gradual diffusion of the fat granules, and the establishment of streaming movement in the protoplasm. Ultimately the granules dissolve and almost entirely disappear, and the conidium, now full of shining, active protoplasm, emits a germinal tube. The latter grows and ramifies rapidly if the surrounding fluid contains sufficient nutritive material, and within the course of a few hours gives rise to an abundant mycelium. Where the fluid is deficient in nutritive material, the mycelial development undergoes various modifications, and where nutritive material is absent, as in distilled water, many conidia refuse to germinate; and, in those cases where germination occurs, the germinal tubes are abortive, their growth being arrested so soon as the store material of the parent conidia is exhausted. The mere addition of moisture is sufficient to induce germination in many fungal spores and conidia, but where nutritive material is wanting, or where the means providing for its assimilation are absent, the amount of growth which takes place is determined by the amount of material stored up in the reproductive body. The phenomena observed in regard to the conidia of Choanephora afford an example of the result of absence of nutritive material, whilst those recorded regarding the germination of lichen-spores apart from algal elements appear to be referable to absence of assimilative capacity.

Characters of the healthy germinal tubes and mycelia.

The germinal tubes and actively-growing young mycelial filaments of Choanephora are full of a shining protoplasm, in which sap vacuoles are present in varying numbers. When examined under high powers, the protoplasm presents a dimly clouded aspect, and a small number of brilliant sharply defined granules are seen scattered through it at wide intervals (*vide* Fig. I., A).

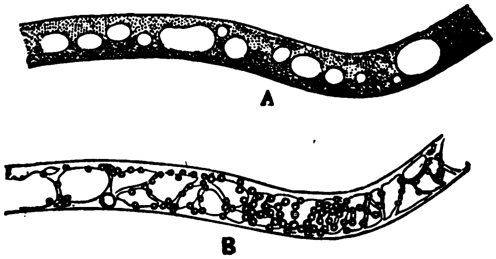

FIG. I.—Germinal Tubes of Choanephora × 1,000.
A, Healthy tube. B, Starved tube.

In such tubes it is almost impossible to detect any movement in the protoplasm, as, owing to the fullness of the tube and the general absence of distinct granules, there is nothing to serve as an index of movement save the slow changes in the form and distribution of the vacuoles. In older portions of mycelium, however, an abundance of granular matter accumulates, and here active streaming of the protoplasm is very distinct in many cases. Granular accumulation increases rapidly preparatory to the development of the fertile filaments, and these and the young conidia arising from them are densely packed with coarsely granular matter.

Nature and origin of the granular matter in old mycelial filaments.

This granular matter may be determined to be of an oily nature by the use of appropriate re-agents, and its appearance in the fructifying mycelia and filaments of fungi is a phenomenon of frequent occurrence. It is usually ascribed to accumulation of oily matter derived from the nutritive medium, and to this, no doubt, it may in many cases be in great part due, but that it is entirely and invariably to be accounted for in this way is rendered very questionable by the phenomena which will presently be recorded as occurring in the protoplasm of starved mycelia. An excessive supply of nutritive material is certainly not favourable to the development of fructification, for where a portion of mycelium is retained in a concentrated and frequently renewed nutritive medium, the appearance of fertile filaments is indefinitely delayed, and the mycelium continues to grow luxuriantly, while a crop of reproductive bodies may generally be readily secured from it by diluting the medium or ceasing to renew it, and thereby allowing its nutritive properties to become exhausted.

Forms of fructification determined by conditions of nutrition.

Various other remarkable effects are produced by variations in the amount of nutritive supply, the special form assumed by the fructification in any cultivation being to a great extent directly determined by the quantity and quality of the nutritive medium. These will be referred to again in the descriptions of the effects of starvation of the mycelium, and a detailed account of them would occupy more space than can be devoted to it here. The general points to be borne in mind are—*1st,* that during the evolution of the young plants from the reproductive cells there is an involution and disappearance of oily matter; *2nd,* that in young mycelia, in which vegetative growth is at a maximum and nutrition most abundant, the protoplasm contains a minimum of differentiated oily matter; *3rd,* that in older mycelia, and specially in the fructifying filaments and young reproductive bodies, a great accumulation of oily matter occurs; *4th,* that excessive nutrition appears to be antagonistic to the development of reproductive bodies.

Keeping these facts in view, the phenomena attending diminution, or deprivation of nutritive material, may now be described. The experiments

Experiments on starvation referable to three subdivisions.

regarding these may be referred to the following subdivisions :—*1st,* Cultivations of conidia in distilled water; *2nd,* Cultivations of germinal filaments in distilled water; *3rd,* Cultivations of more or less developed mycelia in distilled water.

Cultivations of conidia.

1st, Cultivations of conidia in distilled water.—In many cases, as previously mentioned, the conidia refused to germinate at all, while their contents became gradually resolved into a mere loose aggregation of granular matter. In other instances, however, germination occurred. Evolution in such cases was limited to the development of short germinal tubes, and no formation of mycelium ever ensued. The germinal tubes having been formed, two final results occurred. These consisted either in a granular disintegration of the protoplasm, or in the formation of chlamydosporic reproductive bodies. In the one case the contents of the tubes ultimately consisted of a collection of swarming oil granules; in the other they became condensed into shining, isolated masses of oval or fusiform outline consisting of dense aggregations of protoplasmic material, invested by a limiting layer, and in other respects resembling similar reproductive bodies occurring in other mucorine fungi.

Cultivations of germinal tubes.

2nd, Cultivations of germinal tubes.—In this case the conidia were introduced into nutritive fluid, and, at the close of some hours, when germination had freely taken place, the fluid was washed out and replaced by distilled water. The healthy germinal tubes (*vide* Fig. I, A) contain an abundance of dimly clouded protoplasm, with numerous vacuoles and a few distinct granules. The primary effect of the substitution of water for the nutritive fluid is a great increase in vacuolation, the protoplasm becoming contracted as absorption progresses, and ultimately in the majority of tubes being reduced to an irregular peripheral layer, lining the walls of the tubes, and to a series of connecting processes extending across the cavity and forming irregular anastomoses with the lining layer. Whilst these changes occur in the distribution of the protoplasm, another series of alterations affect its composition. The number of granules present in it, which originally is very small, rapidly increases, and this increase combines with the altered arrangement in distribution to render the streaming motion of the protoplasm very evident, as the granules are hurried along the peripheral layer and reticular processes. The granules continue to increase in size and number, and assume a more or less distinctly oily aspect, and after the lapse of a few hours are very abundant and conspicuous. After twelve hours of starvation all protoplasmic activity has ceased in most of the tubes, and the contents are now represented by a mere network of filaments studded with bright granules (Fig. I, B), but in some instances movement continues with great vigour, and is rendered particularly clear by the abundance and size of the granules. Finally, however, movement ceases in these tubes also, and they come to present the same appearances as the others. The peripheral layer of protoplasm appears to become gradually detached from the walls of the tube, so that the contents become reduced to a mere tangled aggregation of filaments and granules. Eventually the connecting material disappears, and the granules swarm free in the tube cavity, or unite into large oil globules which may be dissolved out in ether, and are re-deposited as globules and fat crystals on the evaporation of the re-agent.

Cultivations of mycelium.

3rd, Cultivations of mycelium in distilled water.—The procedure followed in these experiments was similar to that in the case of those with the germinal tubes; the only difference lying in the fact that here the fungal elements were allowed to remain in the nutritive medium for a longer period, and until a considerable development of mycelium had occurred. As a rule, whilst the nutritive fluid was replaced by water in three or four hours from the period at which the conidia were sown in the experiments on the germinal tubes, the substitution was not carried out here until after the lapse of eight or ten hours. The primary effects of the treatment in the present series were identical with those described as occurring in the former one, but while in that series the process ran rapidly through various stages of fatty transformation and disintegration without the occurrence of any further development, one result of depriving a formed mycelium of nutritive material is almost invariably the development of fructification within the course of the next twelve hours.

Sporangial form of fructification characteristic of the starved mycelia.

The form of fructification characterising such cultivations is sporangial. As a result of previous experience, this form had been determined in the case of Choanephora to be developed under circumstances of defective nutrition dependent on various causes—on disproportion between the numbers of conidia sown in a nutritive fluid and its amount, on employing a fluid which was originally weak or had become exhausted by previous cultivations, &c.; but no other procedure appears to afford such certain production of a crop of sporangia. Where the mycelial filaments have not been entirely emptied of their contents during this development, the condition of these is identical with that occurring in the case of germinal tubes which have been exposed to starvation for a similar period, and the development is probably to be ascribed to a utilisation by one portion of the protoplasm of materials derived from the disintegration of another portion.

General results of experiment; fatty change and development of reproductive bodies.

In all three series of experiments the results were similar in shewing that fatty change and ultimate disintegration of the protoplasm are direct results of insufficient nutrition. The development of reproductive bodies coincidently with these processes is very interesting, but by no means so anomalous as it might at first sight appear. There are many facts shewing that the antagonism between individual growth and reproduction is not to be ascribed solely to expenditure in one direction counterbalancing that in another. Root-pruning and poor soil will often force plants into flower and fruit, which, with a liberal supply of nutritive material, have persisted in mere continuous vegetative growth. This, however, is a subject hardly calling for detailed discussion here, but it is of importance to note that the coincidence of the formation of reproductive bodies with an oily condition of the protoplasm is of very frequent occurrence in fungi, and that the present experiments demonstrate that the presence of oil in such cases cannot be taken as necessarily indicative of excessive accumulation of nutritive material.

Experiments on Pilobolus crystallinus.

The other plant in which the effects of insufficient nutrition were studied,—*Pilobolus crystallinus*,—is in various respects not such a good subject for experiment. It cannot be satisfactorily cultivated in a medium allowing of continuous study without disturbance of the growing tissues; it is impossible without great interference with and injury to the growing tissues to free them completely from extraneous matters from which they may derive nutrition; and the healthy growing protoplasm in almost any case contains a considerable amount of differentiated oily matter. Allowing for these drawbacks, the experiments yielded results essentially similar to those in regard to Choanephora.

Source of materials and general nature of results.

The materials for cultivation were furnished by the spores of the plant developed under natural conditions. The spores are at any time readily attainable in Calcutta, as portions of fresh cowdung kept for a day or two in a moist chamber hardly ever fail to produce an abundant crop of the fungus. Fresh spore masses, secured shortly after their discharge from the summits of the parent filaments, were introduced into cowdung, which had been diluted with water and subsequently boiled to secure the destruction of extraneous fungal elements. By this means a clean crop of Pilobolus was secured, developed in a basis sufficiently fluid to render the removal of germinating spores or mycelial filaments an easy matter. In removing mycelia it was found impossible to free the filaments entirely from adherent portions of the basis without injuring them so greatly as to complicate the results of experiment, but the amount of nutritive material was reduced to a minimum by the adoption of the following method. A mass of the cowdung containing mycelium was carefully removed, and introduced into a watch-glass containing distilled water. Gentle agitation served to wash out much of the cowdung; the water was then poured off and replaced by a fresh supply, renewed agitation applied, and this process being repeated several times, the mycelium was at last obtained relatively free from adherent particles. It was then allowed to remain in distilled water, and the phenomena presented by it, at various intervals from the commencement of the experiment, carefully studied. As in the case of the other species, the main effect following the deprivation of nutritive material seemed to lie in an oily transformation in the protoplasm, and the ultimate reduction of the contents of the filaments to mere accumulations of swarming fat granules. The nature of these granules can generally be readily determined by the action of appropriate re-agents, and the quantities of yellow oil which can be extracted is very remarkable.

Spores of Pilobolus refuse to germinate in distilled water.

The spores of Pilobolus, as a rule, entirely refuse to germinate in distilled water, and the contents merely pass on into granular degeneration.

General results of starvation of vegetable protoplasm.

In these experiments on vegetable tissues the primary effect of starvation seems to consist in a gradual analysis of the complex amalgam constituting the protoplasm, and of a precipitation of oily matter from it. This is followed by transformation affecting the albuminoid constituents, and ultimately leading to their more or less complete conversion into fat. Vegetable protoplasm, according to most recent observations, consists of "a combination of albuminous substances with water and small quantities of incombustible material. In most cases it also contains, as may be concluded on physiological grounds, considerable quantities of other organic compounds, belonging probably to the series of carbo-hydrates and fats. These admixtures are distributed through its mass in an invisible form."[1]

The rapidity with which oil granules appear in many instances renders it probable that those first produced are the result of a separation of pre-existent oil. That the oily material subsequently produced is a new formation is demonstrated by the entire disappearance of all other elements from the interior of the cells or filaments.

Contrasted phenomena of evolution and involution.

The contrast between the phenomena attending evolution and involution is strikingly exhibited in these experiments. In germinating spores we find a solution and disappearance of differentiated oily matter; in starved filaments, a precipitation of oily matter from a previously homogeneous protoplasm.

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[1] Text Book of Botany, Morphological and Physiological, by Julius Sachs. Translated and annotated by A. W. Bennett and W. T. Thistleton Dyer. Oxford, 1875, p. 37.

CHAPTER II.

EXPERIMENTS ON THE EFFECTS OF DEFICIENT SUPPLY OF NUTRITIVE MATERIAL ON ANIMAL TISSUES.

Animals employed in experiment: Amphibian larvæ.

THE animals employed in the experiments on this point were the larvæ of the common toad of this part of India (*Bufo melanostictus*) and of *Rana tigrina*, the so-called Bullfrog of Anglo-Indians. The procedure followed consisted in retaining the larvæ in water containing varying amounts of nutritive material, or, as far as possible, entirely devoid of it; freshly distilled water being employed in the latter case, as in the experiments on starvation of fungal tissues. A very large number of careful observations were made on the toad-larvæ, those on the larvæ of the bullfrog were few in number, and only undertaken with a view to compare the general results with those of the former series. A detailed account will therefore be given regarding the phenomena observed in the toad-larvæ with brief notices of those occurring in the others.

An acquaintance with healthy tissues and organs necessary to the appreciation of the effects of abnormal conditions.

Before describing the effects produced by abnormal conditions of nutrition it is necessary that some account of the healthy tissues and organs should be given. A complete description of the entire anatomy of the larvæ would occupy much space, and seems unnecessary for a correct apprehension of the most important effects of starvation; anatomical details are therefore given in regard only to the transparent portions of the tail, and to the intestinal canal. The state of the tissues in these was made the object of special study in all the experiments, the tissues of the fin affording exceptionally favourable opportunities for observations conducted during the life of the animals, and those of the intestinal canal being readily studied without the employment of means calculated to introduce manipulative fallacies.

Structure of the fin of the larvæ of "Bufo melanostictus."

The lateral portions of the tail in the larvæ of *Bufo melanostictus* may be described in general terms as consisting of a sheath of epidermis containing a network of ramified connective tissue elements, together with vascular and nervous structures, and a number of free cells or bioplasts characterised by their irregular ramified outline and amœboid changes of form. A few cells containing pigment are also present in some cases, but their number and distribution are very uncertain.

Double layer of epidermal cells.

The epidermis consists of two layers of epithelial cells. In the outer of these layers the constituent cells are flattened, so as to form polygonal plates. The edges of these plates are straight, or at utmost only shew slight shallow sinuosities (*vide* Fig. II, A).

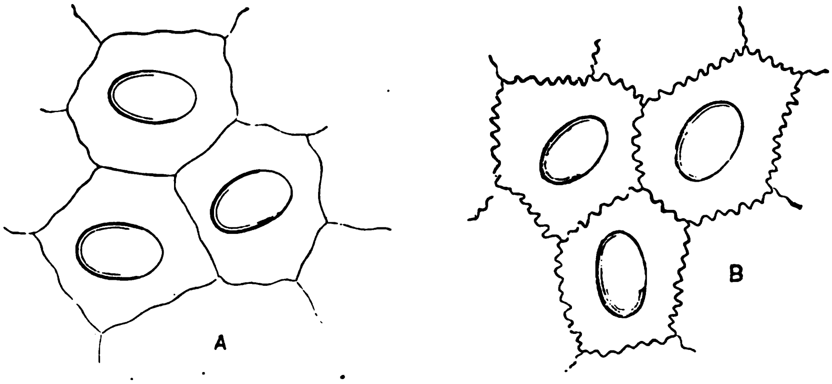

Fig. II.—Epidermal Cells × 1,000.
A, Cells of superficial Layer. B, Cells of deep Layer.

The cells vary greatly in size and form in various portions of the fin, but are apparently everywhere closely adapted to one another, forming a continuous, uninterrupted sheath over the deeper structures. Each cell contains a large oval nucleus, and this, together with the portion of the cell immediately surrounding it, appears to project on the under surface of the plate. Due to this circumstance, whilst the external surface of the entire layer of epithelium is flat and smooth, the under surface is uneven and covered with prominences. These prominences come into close contact with the upper surface of the inner layer of epidermis, while a series of shallow spaces is left elsewhere corresponding with the thin portions of the plates.

Description of the deeper layer of cells.

The inner layer of epidermis differs in many respects from that just described. The cells of which it is mainly composed resemble those of the outer layer in their polygonal outlines, and in the size and form of their nuclei. They are not, however, nearly so flat and thin, but present a tabular in place of a scale-like form, each cell being of some depth, and more or less convex inferiorly. The margins of the cells are deeply and closely sinuate, the prominences and depressions of neighbouring cells being closely adapted to one another (*vide* Fig. II, B). There is not the same uniformity throughout the whole extent of this layer of the epidermis as in the case of the outer layer. Intercalated among the cells which have just been described are cell spaces, which stand out conspicuously, due to their dark granular contents, and, as a rule, considerably exceed the surrounding cells in size (*vide* Fig. III).

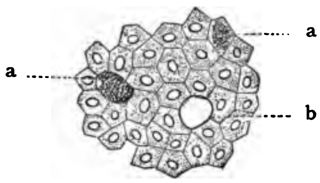

Fig. III.—Deep Layer of Epidermis × 180.
a, a, Granule cells. b, Empty cell-space.

The granules with which they are filled vary somewhat in size in different cases, in some being very coarse, and in others fine and molecular; when in mass they appear of a dark yellow or brown colour. In addition to these cells or cell spaces, for in many instances there seems to be no evidence of any distinct cell membrane, blank spaces or hiatuses in the continuity of the layer of cells present themselves here and there, which in size and form so exactly resemble the cells containing the granular matter as at once to suggest the idea that they owe their origin to the discharge of the contents from such structures.

Granule cells: their nature and development.

The nature of the contents and the phenomena of development of these granule cells was carefully investigated, and I believe that there can be no doubt that they are merely epithelial cells which have undergone fatty change and which are ultimately removed to make room for new structures. At first sight they recall the "Schleimzellen" originally observed by Leydig in the integument of fish and amphibia, and subsequently described by various other authors, and specially by Franz Schultze and Langerhans.[1] Such cells are generally regarded as unicellular glands, which, according to some observers, discharge their secretion on the surface; according to others they never reach the surface, but by means of their thick mucoid secretion assist in effecting the desquamation of the older layers of epidermis. The granule cells in the present case resemble the "Schleimzellen" in being modified epithelial cells, but here the resemblance ceases. They differ entirely from the "Schleimzellen" in the nature of their contents; they cannot be regarded as unicellular glands unless all cells normally undergoing degeneration and destruction are to be regarded as such, and they certainly do not serve to facilitate desquamation, as they may be developed and ultimately disappear in excessive numbers without any tendency to desquamation.

They contain oily matter.

The nature of the granular matter is easily determined by means of alcohol and ether, the granules being completely and rapidly dissolved under the influence of these re-agents. The first effect of the solvents is to cause active swarming of the granules, which either melt together into larger granules and globules previous to dissolving, or merely vanish, of a sudden, without the occurrence of such a process. The swarming granules occasionally become dispersed ere dissolving and spread for some distance in the interspaces between the two layers of epidermis; but I have never seen them discharged externally, even where the parent cells have been so much distended as to cause elevations of the surface. After the dissolution of the granules open spaces are left in the deeper layer of epidermis precisely similar to those occurring normally in it, save in cases where the cells have only undergone partial transformation ere the application of the re-agents, when traces of an atrophied cell-wall and nucleus are more or less distinctly recognisable in the spaces.

Stages in the development of granule cells.

It is easy to trace the various stages of transition by which the normal epidermal cells are transformed into mature granule cells. The earliest symptom of impending transformation consists in an increased refractiveness and density of the cell contents. They acquire a yellowish tint, granules begin to appear and, continuing to accumulate, form a dense yellow or brown mass, which ultimately occupies the entire cell cavity (*vide* Fig. IV, A & B).

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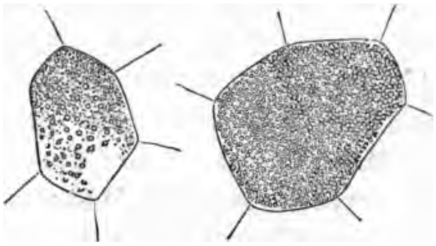
[1] "Ueber die Haut einiger Süsswasserfische." Von Dr. Franz Leydig. Zeitschrift für wissenschaftliche Zoologie, Bd. III, S. 2, 1851.

"Ueber Organe eines sechsten sinnes." Von Dr. Franz Leydig. Verhandlungen der Kaiserlichen Leopoldino-Carolinischen deutschen Akademie der Naturforscher, Bd XXXIV, Dresden, 1868.

"Epithel-und Drüsen-Zellen," Von Franz Eilhard Schultze. Archiv für Mikroskopische Anatomie, Bd. III, S. 137, 1867.

"Ueber die Haut der Larve von Salamandra maculosa." Von Dr. Paul Langerhans. Archiv für Mikroskopische Anatomie, Bd. IX, S. 745.



A B

FIG. IV.—Stages in the development of granule cells × 1,000. A, Young cell. B, Fully developed cell.

During this accumulation the cell generally increases considerably in size, so as to fill a space twice or three times as great as that which it originally occupied, and the nucleus is at the same time pressed to one or other side of the cell. After the highest stage of development has been attained, a certain amount of condensation usually occurs, and the granular mass shrinks and lies more or less free in the space which it formerly occupied. The nucleus and cell-wall finally disappear, and a mere mass of fat granules remains behind, lying in a large space in the epidermal tissue. Such appears to be the normal course of development of these structures, but in some cases more or less pigment is deposited along with the fat, and persists after the solution of the latter.

They differ from the cells described by Kolliker.

The only other bodies which these cells in some degree resemble are the granule-cells discovered by Kölliker in the epidermis of the lamprey. They differ from them, however, in their simple structure, having no processes connected with them which can be regarded either as gland ducts (Kölliker) or sensory filaments (F. Schultze).

Probable functions of the granule cells.

In the normal state of the healthy larvæ, the granule cells are developed in varying, but never in excessive numbers. In so far as a careful study of their development and subsequent history affords any information on their functions they appear to subserve important ends in the processes of growth of the tissue in which they occur, as well as in the involution of those portions of the latter which are peculiar to the larval condition, and disappear on the assumption of the adult form. As previously mentioned, the granule cells during the course of their development increase considerably in size, forcing apart the surrounding cells of the epidermis, and, on their dissolution, leaving spaces much larger than those occupied by the unaltered elements of the tissue. Under normal conditions these spaces are now filled up from below by the intercalation of new structures. These may in some cases be derived from the system of sub-epidermal free amœboid cells; but, as a rule, they are, I believe, derived from the connective tissue system. I have frequently been able to trace a direct connection between fusiform nuclear bodies lying in the blank spaces and the common connective tissue system of the interior of the fin; and in cases where this cannot be done, the appearances presented by the new elements in spaces which are about to be filled up cannot fail to render such an explanation of their origin probable. The peripheral ramifications of the connective tissue appear to be everywhere closely connected with the inner surface of the epidermis, a system of connective tissue corpuscles lying scattered over the latter, while many processes appear to be directly affixed to the epidermal cells themselves. On the formation of a blank space or hiatus in the epidermis, one or more connective tissue corpuscles, according to the size of the area to be filled up, are drawn into it. The connective tissue elements at first form an open reticular tissue, which, as the nuclei enlarge and the processes diminish, is gradually converted into a coherent patch of new cells intercalated among the older epidermal elements, and occupying a space originally formed by the degeneration and removal of one cell. If this interpretation of the phenomena be correct, one main function of the granule cells under ordinary circumstances is mechanically to enlarge the area of the inner layer of the epidermis.

Probable method by which the outer layer of epidermis is accommodated to variations in the area of the inner layer.

Observations did not decide how the outer epidermal layer accommodates itself to the increased area of the inner one. The occurrence of any general desquamation was never observed, and there were no appearances of the addition of new elements from beneath. From the extreme variations in the form and size of the cells of the outer layer it seems not improbable that a good deal of the accommodation is accomplished by means of mere extension and flattening of the constituent cells.

ule cells probably play an
ant part during the resorp-
t the fin.

t is evident that the granule cells may also play an important part during the resorption and disappearance of the fin, for, if developed in large numbers without equivalent addition of new elements from the deeper tissues, y must tend to the ultimate removal of the deep layer of epidermis. This, vever, is a subject not calling for discussion on the present occasion. The portant points to recollect here are, that when developed in due proportion, e granule cells provide for the growth of the tissue in which they occur, and at in such proportion their development is strictly physiological for the rganism, although pathological for the individual cells.

Internal structure of the fin.

The remaining structures in the tail of the larvæ call for little detailed notice, as their characters are familiar to all physiological observers. The branched amœboid cells beneath the epidermis are very inconspicuous during the life of the animal, and may readily escape notice unless carefully looked for (*vide* Fig. V, A).

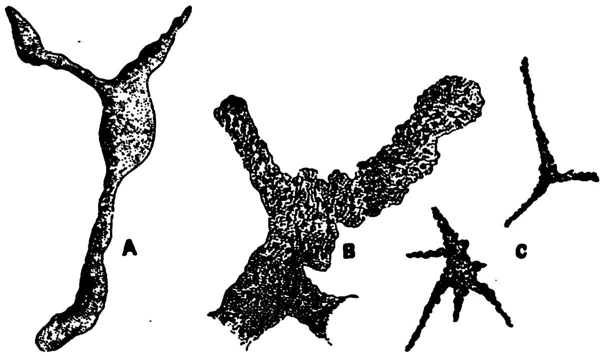


FIG. V.—Amœboid cells. A & B × 1,000, C × 180.
A, Healthy cell. B, Portion of a starved cell. C, Starved cells.

The connective tissue elements present no special peculiarities. The vascular loops are full, and the current of blood is strong and rapid. Many of the blood corpuscles are characterised by containing two or three minute shining oil granules.

This brief account of the normal anatomy of the tissues may serve to render an account of the phenomena associated with deprivation of nutritive material intelligible. The following description is taken from the notes recorde

Notes of the state of the tissues in a case of starvation.

during the examination of a tadpole which had been for a fortnight in distilled water :—"The larva is very feeble and tends to turn over on its back when at rest. The thin portions of the tail to the naked eye appear of a whitish colour in place of presenting the transparent aspect normal to them, and when examined with a simple lens are found to be covered with innumerable white points. Under higher powers these points are resolved into granule cells in various stages of development. Large numbers of fully-matured granule cells are everywhere present, and the number of partially developed ones is very great. Some of the latter are merely beginning to be distinguished from the surrounding epidermal cells by their shining yellowish appearance, while others present various degrees of granular accumulation. The tissue of the deep layer of epidermis appears, as it were, opened out, the constituent cells not being in such close contact with one another as they normally are. Empty granule-cell spaces abound, and here and there large areas occur in which the deeper epidermal tissue is either entirely absent, or replaced by loose reticular tissue consisting of nuclear elements connected together by slender processes (*vide* Fig. VI).

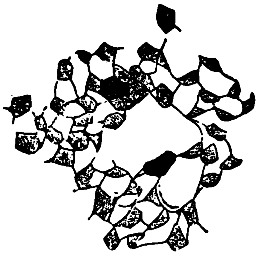


FIG. VI.—Reticular tissue replacing the deep layer of epidermis in a case of starvation × 180.

"Granule cells sometimes occur as it were suspended in the midst of such reticular areas. The outer layer of epidermis appears little affected. There is no opening out of its texture, no hiatuses occur in it, the cells are everywhere closely in contact with one another, and the only abnormal appearances are presented by the nuclei, which in many cases are broken up into a collection of large shining granules. The branched sub-epidermal cells are greatly altered. They have lost their normal soft dim refraction and have become very conspicuous, appearing to be distended with material of a yellow colour and containing numerous refractive granules (Fig. V, B & C). The connective tissue corpuscles appear empty and shrunken, and together with their connecting filaments are in some cases studded with bright granules. The amount of blood in the vessels is very small, the current is very feeble, and the corpuscles appear to escape from the vessels with abnormal readiness. Many vascular loops remain entirely empty for considerable periods at a time, and in others isolated corpuscles slowly follow one another at wide intervals. Almost all the corpuscles are studded with large granules and globules of oil, and many of them are quite bleached and colourless. Some in process of disintegration can only be recognised by means of the characteristic arrangement of the oil globules which they contain, and free oil globules afford evidence of the complete destruction of others. Alcohol and ether produced their ordinary effects on the granule cells, and prolonged application of the same re-agents shewed that the yellow matter and granules with which the subepidermal cells were filled was also of an oily nature. The granules first vanished, and the contents of the cells then gradually escaped as large yellow globules, which gradually dissolved and disappeared. The coarse granules in the nuclei of the outer layer of epidermis seemed to be little, if at all, affected by the re-agents."

General results of observations.

Numerous careful examinations of specimens in all stages of starvation afforded results substantially in accordance with those just recorded; variations in degree of change being naturally present in accordance with the varying periods of starvation. The phenomenon which presented itself most conspicuously and frequently at first was an increase in the number of the granule cells. This increase cannot be ascribed to mere accumulation of the cells formed in normal proportion, but failing to undergo complete transformation, for, *1st*, the increase occurs without any evidence of any equivalent increase in persistence of the cells, blank spaces being present in increased rather than diminished quantity; *2nd*, the increase in number of granule cells is often extremely marked when there has been a very considerable destruction of the epidermal tissue over wide areas. In proportion to the period of starvation there is a steady increase in the number of blanks in the deeper layer of epidermis and of areas occupied by reticular tissue. This tissue, which in areas formed early in the course of starvation is comparatively close and approaches new epithelial tissue more or less nearly in its characters, alters in nature in the later stages. The nuclear bodies are then small and far apart, and the connecting processes proportionately lengthened. Ultimately, in the last stages of inanition, the tissue in many places fails to be developed at all, and large blank spaces are left in which the internal tissues are only covered by the outer epidermal layer.

Increased formation of granule cells and destructive changes in the blood.

The increased formation of granule cells is soon and constantly accompanied by changes in the blood supply. The amount of blood becomes visibly diminished, and the blood current flows with diminished rapidity. The oil granules in the corpuscles increase in size and numbers, so as to present themselves very conspicuously even to low-power observations. The destruction of the corpuscles, however, goes on very gradually until a late stage of starvation, at which it appears to assume a more active course. The colouring matter escapes from the corpuscles, and the latter ultimately break up, setting their contained oil globules free in the serum (*vide* Fig. VII).

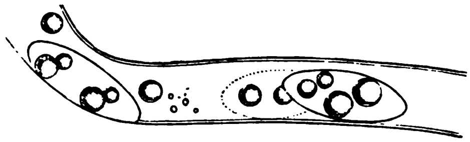


FIG. VII.—State of the blood corpuscles in advanced starvation × 1,000.

Fatty degeneration of the ramified sub-epidermal cells.

Somewhat less constant than either of the above-described phenomena, but yet of very frequent occurrence, is a fatty change in the ramified sub-epidermal, amœboid cells. They increase greatly in size, and appear to become distended with yellow matter and numerous granules. These changes are so conspicuous in many cases as to render the cells one of the most striking features in the starved tissues. The contents of the cells are dissolved out by ether, leaving mere shrunken skeletons behind.

Connective tissue elements little affected.

No such conspicuous changes affect the connective tissue elements even in very advanced stages of starvation. The nuclei lose their plump, shining aspect, and numerous fat granules frequently present themselves, both in them and in the connecting processes, but no great accumulation of fatty matter or destructive change seems to occur.

Fatty change in the living material of the tissues the most conspicuous effect of defective nutritive supply.

The principal effect of defective nutritive supply on the tissues in these experiments, as in those in regard to vegetable tissues, seemed to lie in a fatty change. This change or degeneration specially affected epithelial elements containing a large proportion of living material, and the blood cells. The destructive changes in the blood cells must be regarded as a direct effect of defective nutrition, but it is not easy to determine how far the changes in the epithelial tissues are to be ascribed to this and how far to defective oxidation and consequent accumulation dependent on the changes in the blood. The persistence of the outer epidermal layer is very remarkable, and is probably to be ascribed to the extent to which it is composed of formed, more or less cuticularised material.

Normal anatomy of the intestinal canal in the larvæ.

The normal anatomy of the intestinal canal and the changes occurring in it during starvation remain now to be described. The intestinal canal of the larvæ is of such simple structure and such transparent texture as greatly to facilitate the determination of these. All the structures can be readily subjected to observation without disturbing their normal relations, or interfering with the intestine in any way beyond removing it from the body of the animal. In normal healthy specimens the spiral coil of the intestine appears conspicuous externally, shining through the transparent abdominal walls. It consists of three coats, the external of which is muscular, the internal epithelial, and the intermediate one composed of reticulate adenoid tissue (*vide* Fig. VIII).

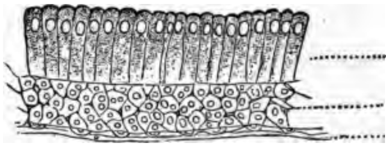


Fig. VIII.—Normal structure of the coats of the intestine × 180.

Muscular, adenoid and epithelial coats.

The muscular coat consists of the two layers of fibres, those in the outer layer running parallel to the length of the canal, those in the inner transversely arranged. The epithelial coat is composed of large cylindrical cells. These call for no special note, as they closely resemble those occurring in the intestines of other animals. Their contents consist of soft, clouded protoplasm with a few scattered granules, and their only peculiarity lies in the fact that their inner, free extremities do not present such a distinctly defined border as that apparent in many intestinal epithelia. The reticular layer between the other coats is formed of a network of fine filaments, the meshes of which are occupied by free nuclear bodies. It is very thin, and under normal circumstances is very inconspicuous, lying as it were compressed between the other two coats. When the latter, however, are separated from one another by pressure, or by means of re-agents which cause the inner one to contract, the meshes of the reticular tissue are stretched and open out, shewing that in many places several strata of reticula are present. In some places, on the other hand, there appears to be only a single layer, the bands of tissue seeming to pass direct from the inner surface of the muscular coat to the outer surface of the epithelial one. Fig. VIII represents a specimen in which several strata of reticula and nuclei are present. The nuclei are plump and shining, and after treatment with alcohol appear softly molecular.

Appearances of the intestine in an advanced case of starvation.

The appearances presented by the intestinal canal of a larva in the last stage of starvation were the following:—"The intestine cannot be detected from the exterior of the abdomen, and on its removal from the body it is seen to be very slender and short. The canal is quite empty throughout almost its entire length, but here and there an isolated brownish yellow granular mass is present. The epithelial coat is everywhere entirely wanting. The reticula of the adenoid coat appear not to have been in any way affected, but the nuclear elements present most abnormal appearances. In place of being quite colourless and smooth, they are rendered extremely conspicuous by being of various shades of yellow and brown due to the presence of accumulations of granular matter within them. In some places comparatively few nuclei are present, and the reticula are empty or contain collections of free granules. The changes in the adenoid tissue are most marked in the upper portion of the intestinal canal, and in the large intestine a large number of unaltered nuclei are still present. On treating the specimen with alcohol and ether, active swarming of the granules in the reticular meshes and in the nuclei occurred; and on continuing the application of ether, many of the nuclei and nuclear masses were entirely broken up, all the yellow matter being dissolved, and disappearing, while an abundance of deep brown pigment granules remained behind. Many of the pigment granules lay loose in the reticular spaces, but others were contained within nuclei, or formed dense aggregations corresponding apparently with nuclei which they had replaced. The yellow granular matter was also dissolved out from he masses of intestinal contents, and the oil thus extracted was subsequently precipitated in the form of abundant oil globules and crystals."

Ultimate effects of starvation on the intestines.

The phenomena presented in this case were not peculiar to it, but may be taken as fairly typical of the intestinal canal in advanced stages of starvation. They shew the ultimate effects of starvation to consist in general atrophy of the intestine, entire removal of the epithelial coat, and extensive degeneration and destruction of the nuclei of the adenoid tissue. The degree of general atrophy may be estimated from the fact that, while in the healthy tadpoles which were examined, the average length of the intestine from the liver to the commencement of the large intestine was 1·36 inch, and its average breadth 0·018 inch, in the starved specimens the corresponding averages were only 0·57 and 0·011 inch.

Absence of epithelium invariable.

The absence of epithelium appears to be invariable in cases of advanced starvation, and in them the destructive change has generally been so complete as to leave no evidences capable of explaining by what processes it has been effected. Careful observations on specimens in earlier stages of starvation, however, clearly determined that they essentially consist in a fatty transformation of the contents of the cells, followed by gradual atrophy and disappearance of the tissue which they compose. Even after very brief periods of deficient nutrition, changes begin to manifest themselves in the cells. The processes of change do not, however, affect the entire extent of the epithelial surface simultaneously. They first declare themselves over an area extending from a point at some distance from the upper extremity of the small intestine to another towards its lower extremity. From this area the changes spread gradually both upwards and downwards; but, until the epithelium has entirely disappeared, differences in the degree of change can be distinctly traced in various regions, and the area primarily affected is often entirely denuded at a time when the terminal portions of the small intestine and the whole of the large one shew a considerable amount of recognisable epithelium.

First indications of change in the epithelial coat.

The first sign of change is shewn by the cells acquiring a yellow tint towards their free extremities. This tint soon becomes very marked, and forms a distinct coloured band along the margin of the epithelial coat when viewed sectionally. The colouring is due to the accumulation of a thick granular matter within the cells, which is first deposited immediately around the nucleus, and gradually spreads thence throughout the cell. It consists of fat which can be dissolved out by treatment with alcohol and ether. With regard to the precise nature of the process by means of which the altered cells are finally removed, I am unable to give any definite opinion. During the advance of the transformation over an area of epithelium the thickness of the layer of cells seems gradually to diminish until, just before the complete disappearance of the coat, it is represented by a mere narrow granular, yellow band on the surface of the reticular tissue; but whether the individual cells are gradually atrophied and consumed away, or whether the phenomena are due to the process first affecting the largest, fully developed cells, and subsequent to their destruction, invading younger less developed structures, I was unable to determine. Whatever the precise nature of the process may be, its ultimate effect is undoubtedly an entire destruction of the epithelium (*vide* Fig. IX).

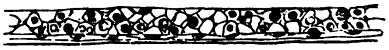


FIG. IX.—Coats of the intestine in advanced starvation, shewing complete absence of epithelium × 180.

The débris of the destroyed tissue appears in great part to enter the cavity of the gut, and passes on to form an important constituent in the evacuations which continue to be passed in perceptible amount up to the latest stages of starvation. Careful examinations were, on several occasions, made of these excreta. They consisted, in great part, of amorphous particles probably derived from dust which had entered the fluid, but they always contained considerable quantities of soluble oily matter. The infusoria, too, which are almost invariably present in the intestinal canals of the larvæ, were generally full of oil globules and granules in cases where their host had been starved.

Nature of the changes in the adenoid coat of the intestine.

The changes in the nuclear elements of the reticular tissue are always extremely marked. As in the degeneration of the epithelium, the process of change does not appear to occur simultaneously over the entire extent of the intestine, and as it does not go on to complete destruction and removal of the tissue, differences in the degree of affection in different portions of the intestinal surface are evident, even in the last stages of starvation. In this coat the changes seem to occur first, and to attain their highest development in the upper portion of the canal, while in other parts in proportion to their distance from this portion they appear r and are less complete. The earliest symptom of change here also is a nge in the colour of the affected structures. The nuclei, in place of present- their normal soft, colourless appearance (*vide* Fig. X), assume a yellow

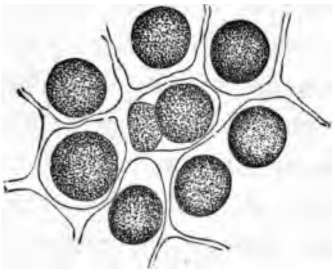


FIG. X.—Healthy nuclei of the adenoid tissue × 1,000.

our, and become distended with a thick yellow material. This material some cases is distinctly granular, but in others it appears rather as though were a thick fluid. As the change continues, the nucleus appears to become verted into a mere aggregation of this substance; and judging from the sence of free granules and masses of it in the meshes of the tissue, the cess seems in many cases to end by the breaking up of the mass. The terial, like that in the altered epithelium, can be readily determined to of an oily nature.

In the earlier stages of starvation such material alone is deposited in the clei; but in the later stages of the process it is apparently invariably associ- d with more or less pigmentary deposit. The amount of pigment varies greatly in different cases,—in some being comparatively scanty, in others so excessive as to form the most conspicuous feature in the tissue, and greatly obscure the fatty deposit with which it is associated (*vide* Fig. XI).

gment deposited in the nuclei sequent to the occurrence of fat- hanges.

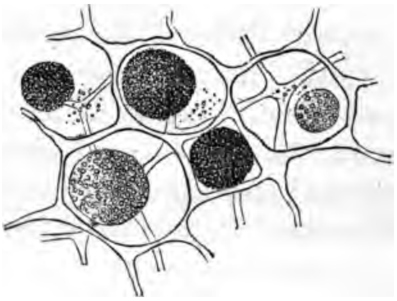


FIG. XI.—Appearances of the nuclei of the adenoid tissue in a case of advanced starvation × 1,000.

Its distribution over the intestinal surface is similar to that of the fatty deposit,—the upper portion of the small intestine being the most constant site of its extensive occurrence. In some cases the nuclei appear to be reduced to mere masses of pigment granules, and numerous free granules lie loose in the meshes of the tissue.

Probable origin of the pigmentary deposit.

This extensive deposit of pigment is probably due to the great destruction of blood-corpuscles accompanying starvation. The time of its appearance coincides with that period of starvation in which distinct evidences of considerable destruction in the blood present themselves; and observation seemed even to indicate a certain amount of correspondence between the degree of blood-destruction and of pigmentation in individual cases.

Effects of starvation on the liver.

Starvation also produced most marked effects on the liver. The size of the organ is greatly diminished; it assumes a dark brown colour in place of the pinkish-yellow tint, normal to it; and its substance appears granular. When examined microscopically it is found to be bloodless, and its substance reduced to a mere amorphous mass of dark yellow and brown oil-granules, with a sprinkling of bright red concretions scattered through it in some cases. The gall bladder is invariably full, and very frequently is greatly distended. The contained fluid, in place of being almost colourless, as it ought to be, is green. The depth of the colour varies considerably, but in some cases is so intense as to cause the gall bladder to appear as a deep emerald-green body which shines prominently through the abdominal walls. The gall bladder, in any case, usually contains some fatty concretionary matter; but in starved cases this is present in excessive quantity, and is frequently of a deep green colour.

General results of starvation in the various tissues of the larvæ.

In the case of the intestine, as in that of the tail of the larvæ, the ultimate effect of starvation consisted in a destruction of tissue associated with fatty change and subsequent disintegration of the component elements. The principal difference between the two cases was one of degree rather than of kind,—the amount of destruction in the intestinal tissue being much greater than that in the tail. In both cases the destructive changes were specially manifest in active epithelial elements, that is, in structures in which the living protoplasm bore a high proportion to the amount of formed material. The occurrence of fatty change in the free sub-epidermal cells finds a parallel in that presenting itself in the clear elements of the adenoid tissue of the intestine, and in both cases the nnective tissue structures were little affected and remained persistent after occurrence of extensive destruction in other parts. The phenomena in both es, and specially those occurring in the intestinal canal, shew conclusively t during the course of starvation the changes are not limited to mere atrophy, t that in some tissues extensive destruction of the component elements urs rendering the latter incapable of recovery on the subsequent addition nutritive supply. So long as any living material remains within the affected ments the possibility of recovery remains; but when they have absolutely oken up, or where they are converted into mere aggregations of dead matter, s clear that restoration of the tissue of which they form a constituent can y be effected by the formation of new elements.

It is also clear that the amount of transformation of tissue taking place in the organism is not of necessity directly indicated by the mere chemical determination of the amount and nature of the materials leaving the body in the ious excretions, for the products of transformation need not necessarily pass but may accumulate in large quantities, as in the case of the pigmentary l fatty deposits occurring in the intestinal tissue as recorded above.

oring-up of the products iin the organism may mask extent of tissue-change taking e in it.

The experiments which were conducted with larvæ of *Rana tigrina* shewed that in these also the destructive effects of starvation were specially centred on the intestinal ıal, and that the changes in the tissues of the mucous membrane were essenlly similar to those just described.

sults of experiments in the æ of Rana tigrina.

In so far as the present experiments afford any information on the subject changes effected by starvation in animal and vegetable tissues are fundamenty the same, and the variations presented by the phenomena attending the cess in individual cases are mainly dependent on variations in the amount l character of the formed material present. Where this is small the effects of destruction and removal of the protoplasmic constituents are rendered rapidly conspicuous, but where it is present in large amount and is of a reent nature the occurrence of change is to a great extent masked, and large tions of tissue, which, in so far as active function is concerned, have in great asure ceased to serve any purpose in the organism, may, to outward appeare, remain almost unaffected.

fects of starvation on animal vegetable tissues fundament- the same.

CHAPTER III.

PHENOMENA OBSERVED IN THE POST-MORTEM EXAMINATIONS OF CASES OF FAMINE-DIARRHŒA AND DYSENTERY.

Source of data regarding "famine-diarrhœa" and dysentery.

THE data for this chapter were obtained from the careful examination of ten cases of famine-diarrhœa and dysentery. These examinations were conducted in Madras in May and June 1877, at the Monegar Choultry Relief-Camp, and were subsequently supplemented by further investigations of preserved specimens of individual organs and tissues in Calcutta. From the limited number of cases it is necessary to exercise caution in regarding the phenomena presented by them as essential to the disease or as the product of special conditions, and, as will be subsequently shewn, special sources of fallacy exist in regard to certain tissues, in which appearances are liable to be complicated by the nature of the curative treatment. It is under these circumstances that the value of the experimental evidence specially declares itself, by affording an index to the character of the changes which may be regarded as essentially due to defective nutritive supply.

Data obtained from characteristic cases of disease.

All the cases were regarded by the local observers as characteristic specimens of the prevalent forms of disease. The symptoms in most of them had been watched from the beginning, having manifested themselves in the patients after various periods of residence in camp; with one exception they were described as having been ushered in by diarrhœa and ending with more or less pronounced dysenteric symptoms. In the exceptional case the symptoms were of a dysenteric nature throughout. The ages of the individuals could only be approximately determined, but among them there were elderly people, adults in the prime of life, and young children. The autopsies were all made within twelve hours of death, and before any traces of decomposition had manifested themselves. In one of the adults and in all the children there was an almost entire absence of rigor mortis; in the remaining three cases it was well marked. In all emacition was great, and in the majority excessively so, as the following measurements shew :—

Table I.—Measurements in ten cases of Famine-Diarrhœa and Dysentery.

Number of case.	Sex.	Approximate age—years.	Height from heel to vertex.	Girth of chest at axillæ.	Girth of chest at nipples.	Girth of waist.	Girth of arm at thickest part.	Girth of fore-arm at thickest part.	Girth of thigh at thickest part.	Girth of leg at thickest part.
			Inches.	Inches.	Inches.	Inches.	Inches.	Inches.	Inches.	Inches.
1	Female.	60	59·5	27·00	25·00	18·00	5·50	6·25	11·00	8·25
2	Male.	50	72·0	27·50	28·50	?	6·00	6·77	11·62	?
3	„	35	61·0	28·00	28·50	21·00	7·00	7·37	12·12	6·00
4	„	35	63·5	27·00	27·25	20·25	6·77	6·37	11·50	8·25
5	„	6	44·0	19·00	20·00	16·50	4·00	4·50	7·50	5·87
6	„	5	40·5	16·50	18·00	13·50	3·87	4·50	7·50	6·50
7	Female.	3	34·0	13·50	15·50	10·00	2·77	3·25	5·50	4·25
8	Male.	1·25	27·5	14·00	14·87	10·77	3·12	3·87	4·87	3·77
9	Female.	1·25	30·0	12·77	15·00	11·50	3·77	3·87	6·62	5·87
10	„	1	26·5	13·00	14·00	10·25	3·00	3·25	5·00	4·00

Data regarding weight of organs.

The next two tables illustrate various points regarding weights of the bodies and of individual organs; the first shews the actual weights in each case compared with height; the second shews ratios per cent. of weights of various organs on the total body-weight :—

Table II.—Actual Weights of Bodies and Individual Organs.

Number of case.	Sex.	Age.	Total height in inches.	Weights. Body.		Brain.		Heart.		Right lung.		Left lung.		Liver.		Spleen.		Right kidney.		Left kidney.	
				oz.	dr.	oz.	dr.	oz.	dr.	oz.	dr.	oz.	dr.	oz.	dr.	oz.	dr.	oz.	dr.	oz.	dr.
1 . .	Female.	60	59·5	1,000	8	35	0	3	8	15	0	13	0	21	0	1	8	2	8	2	8
2 . .	Male.	50	72·0	1.360	0	44	0	6	0	20	0	14	4	30	0	0	6	2	3	2	2
3 . .	„	35	61·0	1,008	0	41	0	5	0	9	0	9	4	32	0	0	10	3	0	3	2
4 . .	„	35	63·5	1,008	0	40	0	5	8	23	0	8	0	37	8	4	0	3	8	3	8
5 . .	„	6	44·0	496	0	42	0	2	7	6	0	4	8	15	8	1	8	2	0	2	0
6 . .	„	5	40·5	368	0	40	0	1	8	2	8	2	4	8	8	0	8	1	0	1	8
7 . .	Female.	3	34·0	488	0	25	8	1	0	3	8	2	12	9	0	0	8	0	10	0	10
8 . .	Male.	1·25	27·5	180	0	28	0	1	0	2	0	2	0	7	0	0	5·9	0	11	0	11
9 . .	Female.	1·25	30·0	204	0	32	8	0	9·2	1	7	1	8	6	4	0	7·4	0	14	0	14
10 . .	„	1	26·5	160	0	27	0	1	0	1	12	1	12	4	0	0	8·0	0	8	0	8

Table III.—Ratios per cent. of Weights of Individual Organs on Total Body-weight.

Number of case.	Total body weight.		RELATIVE WEIGHTS PER CENT.							
			Brain.	Heart.	Right lung.	Left lung.	Liver.	Spleen.	Right kidney.	Left kidney.
	oz.	dr.								
1 . .	1,000	0	3·5	0·35	1·50	1·30	2·1	0·15	0·25	0·25
2 . .	1,360	0	3·2	0·44	1·40	1·00	2·2	0·027	0·16	0·16
3 . .	1,008	0	4·0	0·49	0·89	0·91	3·1	0·06	0·29	0·31
4 . .	1,008	0	3·9	0·54	2·20	0·79	3·7	0·39	0·34	0·34
5 . .	496	0	8·4	0·49	1·20	0·90	3·1	0 30	0·40	0·40
6 . .	368	0	10·8	0·40	0·67	0·61	2·3	0·13	0·27	0·40
7 . .	488	0	5·2	0·20	0·71	0·56	1·8	0·10	0·12	0·12
8 . .	180	0	15·5	0·55	1·10	1·10	3·8	0·27	0 50	0·50
9 . .	204	0	15·9	0·27	0·70	0·73	3·0	0·22	0·42	0·42
10 . .	160	0	16·8	0·62	1·09	1·09	2·5	0·31	0·31	0·31

Comparison of weights with a standard.

The remaining tables contain a comparison of the weights, total and relative, in cases of famine-diarrhœa and dysentery, with those in other forms of disease. In attempting such a comparison only the adult cases have been taken, as no standard for children was attainable, and the results from them are set against standards obtained by Dr. S. C. Mackenzie, from the examinations of the bodies of 99 native prisoners who died from various causes in the Presidency Jail, Calcutta. The results must of course be accepted with extreme reservation, as the number of the cases is too small to give trustworthy averages; the subjects were natives of a different part of India from that furnishing the standard, and both they, as well as the standard with which they are compared, were persons suffering from disease. So far as I can ascertain, no trustworthy data exist shewing the normal weights of individual organs in healthy natives.

TABLE IV.—*Comparison of Weights in cases of Famine-Diarrhœa and Dysentery with Standard Weights.*

	Total height in inches.	Actual Weights.								
		Body.	Brain.	Heart.	Right lung.	Left lung.	Liver.	Spleen.	Right kidney.	Left kidney.
		oz. dr.	oz. dr.	oz. dr.	oz. dr.	oz. dr.	oz. dr.	oz. dr.	oz. dr.	oz. dr.
Case 1 . . .	59·0	1,000 0	35 0	3 8	15 0	13 0	21 0	1 8	2 8	2 8
Case 2 . . .	72·0	1,360 0	44 0	6 0	20 0	14 4	30 0	0 6	2 3	2 2
Case 3 . . .	61·0	1,008 0	41 0	5 0	9 0	9 4	32 0	0 10	3 0	3 2
Case 4 . . .	63·5	1,008 0	40 0	5 8	23 0	8 0	37 8	4 0	3 8	3 8
Average . . .	64·3	1,094 0	40 0	5 0	16 12	11 2	30 2	1 10	2 12	2 13
Standard . .	64·5	1,777 0	40 12	7 0	14 0	15 0	38 8	7 0	2 12	2 12

TABLE V.—*Relative Weights of Organs to Total Body-weight.*

	Body.	Brain.	Heart.	Right lung.	Left lung.	Liver.	Spleen.	Right kidney.	Left kidney.
Famine-diarrhœa and dysentery	1,094=100	3·65	0·45	1·5	1·0	2·7	0·14	0·25	0·25
Standard . .	1,777=100	2·29	0·39	0·78	0·84	2·16	0·39	0·15	0·15

Phenomena of weight presented by individual organs.

Taking the data as they stand, they shew that the liver, spleen, and heart have sustained considerable loss in actual weight, while the brain and kidneys have remained practically unaffected. The results given by the lungs appear at first sight contradictory,—the right lung shewing a considerable increase in average weight, and the left one an even greater decrease. This anomaly is, however, dependent on the small number of the cases, and is explicable by the fact that, in three out of the four furnishing the average, the right lung was hepatised over considerable areas, whilst the left one was only very slightly affected in this way in any. Taking this into account, the figures seem to shew that, when free of effusion, the lungs also suffer considerable diminution in weight. When the relative weights of individual organs are compared with the total, we find an increase in every case, save that of the spleen. Leaving the right lung out of consideration, the greatest relative increase occurs in the brain and kidneys.

The spleen is the only organ shewing both absolute and relative loss; the liver, heart, and left lung shew absolute loss, but relative gain. The absolute weights of the brain and kidneys remain unchanged; their relative weights are largely increased. The unaltered weight of the brain and the great loss in the spleen are noteworthy as being essentially characteristic of the cases as connected with deficient nutrition. In animals which have been starved to death the spleen is said to lose 71 per cent. in weight—a loss only exceeded by that occurring in the fat and blood—while the nervous system loses only 1·9 per cent., coming lowest in the series of tissues and organs when arranged in order of loss.[1]

Condition of the skin.

In proportion to the amount of emaciation, the skin was loose, and in many places shrivelled or in large lax folds. The surface was harsh and dry, unless inunction of oil had been carried on until immediately before death. Much of the surface, specially about the chest and back, was covered with scurfy flakes of desquamating epithelium, and frequently presented a peculiar sooty darkness, simulating the discoloration due to accumulation of dirt, but in reality dependent on changes in the substance of the epidermal tissue. Both scales and darkened portions of the deeper tissue were subjected to microscopic examination. The scales, as well as flakes of epithelium artificially detached from the surface, were found to consist of very granular epithelial cells. No parasitic organisms were detected, save in proportions in which they may be encountered in any portions of detached epidermis. This is somewhat interesting, as it might have been expected that parasitic organisms would have found conditions specially favourable for development. The greater bulk of the granular matter was of an oily nature.

Fatty condition of the epidermis.

Part of the oil may have been extraneous, and due to the fact that inunction with oil was in many cases specially adopted as a curative measure; but examinations of the deeper portions of the epidermis seem to indicate that a formation of fat had occurred in the tissue itself, many of the epithelial cells in place of undergoing their normal transformations becoming more or less loaded with oily granules. This change was not confined to the epithelial cells of the general surface, but also affected that lining the sweat-glands, the convoluted portions of which were in many cases rendered very conspicuous by the opacity resulting from the granular accumulation. Such changes may to a great extent account for the peculiar phenomena presented by the skin in these and similar cases, the darkened colour and dry harsh condition of the skin being due to alteration in the characters of the cells of the general surface and the impaired function of the glandular tissue, the scaly desquamation to diminished consistence in the deeper layers of epidermis allowing of ready detachment of portions of the older and more resistent, superficial layers in which the cells have undergone their normal development.

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[1] "Principles of Human Physiology." By W. B. Carpenter, M.D., F.R.S., &c. Eighth edition, 1876, p. 108.

Great diminution in amount of subcutaneous fat.

In two of the cases the skin over the feet and ankles was distinctly œdematous. In one case only was there any appreciable quantity of subcutaneous fat; in all the others it was either entirely absent, or present in such extremely small quantity as to be hardly recognisable. The subcutaneous tissue was deeply jaundiced in one case.

State of muscular tissue.

The muscular tissue almost invariably was very pale, and in the majority of the cases it was soft and flabby in consistence.

The state of the heart and pericardium.

The pericardium contained fluid varying in amount from one drachm to one and a half ounces. It was in some cases clear, in others full of minute flocculi. In only two cases was there any considerable amount of fat on the surface of the heart; and in one of these it was closely confined to the neighbourhood of the larger vessels. In several no traces of fat could be detected, and in the rest the amount was very small. In almost every case the muscular tissue was very pale, and in most it was also soft. So yellow was the colour in several cases that it at once suggested the presence of fat; but in only one was there any microscopical evidence of fatty degeneration. This case was No. I of the tables, and the condition was probably connected with the advanced age of the subject, and not due to any special action occurring immediately previous to or during the course of the disease from which death resulted. The right cavities of the heart, as a rule, contained considerable quantities of white or parti-coloured dots; the left cavities were either empty or contained a little dark fluid blood. In Case IV, in which the lower lobe of the right lung was hepatised and covered externally with soft recent lymph, both the right cavities, the pulmonary artery, and the aorta were quite full of parti-coloured coagula.

The lungs were characterised by extreme general pallor and bloodlessness. In three cases considerable portions of the right lung were hepatised, and in all save two isolated patches of deep congestion, in some cases of actual extravasation, occurred in varying numbers throughout the lung substance. In several of the children the substance was in some places collapsed and fleshy. The state of the pulmonary tissues, taken along with the data regarding weight, indicated that a considerable loss of weight had taken place due to diminished blood supply, but that this in some cases had been masked by the coincident occurrence of localised congestions and effusions.

Characters presented by the lungs.

On opening the abdominal cavity the most striking feature which presented itself was the great diminution in the amount of omental and mesenteric fat. In two cases a considerable quantity was still present; in all the others it was either entirely absent, or present only in very small amount, and in the immediate neighbourhood of the larger vessels. The extreme transparency of the membranes, and the consequent accurate definition of the vascular, nervous and absorbent apparatus were very remarkable. The mesenteric veins, as a rule, were almost entirely empty, and the glands appeared as pale, yellowish, flattened knots among the surrounding colourless structures. The stomach and intestinal canal were characterised by excessive pallor. The small intestine was generally collapsed; some portions of it dead-white and opaque, others colourless or slaty, extremely thin, and so transparent that the colour and shape of aggregations of content-materials could be clearly distinguished externally. In such portions the distribution of the tissue of the circular muscular coat was very distinct, and the tube appeared to be denuded of mucous membrane. In one case (No. V) the peritoneal cavity contained nine ounces of pale straw-coloured fluid.

General appearances of the abdominal cavity.

The tongue in some cases was covered with a thick, creamy, white fur; in others this was to a great extent absent, and the surface presented a denuded and raw appearance. Both of these conditions were described as characteristic of the form of disease, and were regarded as indicative of different stages in the morbid process. The majority of the cases admitted into camp, in which the history and general conditions indicated that deprivation of nutritive materials had continued for long, were characterised by presenting the furred condition of the tongue just described.

Condition of the tongue.

In those cases which progressed favourably this gradually diminished and dis- ppeared, leaving the surface in a normal condition; but in bad cases in which iarrhœa and dysentery subsequently set in the fur cleared off, leaving the sur- ace apparently raw and denuded. Numerous careful examinations were made ith a view to determine the nature and origin of these phenomena. The pro- esses giving rise to them, so far as I could ascertain, were analogous to those reviously described as occurring in the epidermis, as well as to those still to be escribed in reference to the intestinal mucous membrane; as in the case of he epidermal tissue there was no evidence of the occurrence of any special arasitic organisms, or of the special prevalence of those forms usually encoun- ered in the locality. The epithelial tissue was very oily, and a true fatty ansformation seemed to affect the cells of the deeper layers of epithelium in reater or less extent, leading to an imperfect development of the growing cells nd ready detachment of those already formed.

he stomach; mucous membrane ft and bloodless.

The mucous membrane of the stomach was, as a rule, dead-white, quite bloodless, soft and pulpy. It appeared as though in a state of anæmic catarrh. In one case por- ons of it were variegated with pale pink markings of relative congestion.

Condition of the duodenum.

The duodenum presented the same general features as the stomach, but the softening of the tissue of the mucous membrane was much more pronounced. Only in one instance d the surface present a normal appearance, and in the majority the mucous embrane appeared to be more or less completely disorganised.

oftening and disintegration of the ucous membrane in the jejunum.

The jejunum presented much the same appearance, but in some instances shewed distinct evidences of disintegration, and dis- appearance of the epithelial coat, together with gmentation and atrophy of the sub-epithelial tissue. In some cases a certain nount of relative congestion appeared in the denuded areas. The pigmentation, here present, caused the surface of the mucous membrane to present a very eculiar aspect, the colouring matter being situated within the villi so as to pear in fine dark points, as though some dark powder had been sprinkled over e surface.

The mucous membrane of the ileum presented even more evident signs of ange. It was generally characterised by extreme bloodlessness, but faint atches of relative congestion were sometimes present. In all cases save one

Extensive destructive changes in the ileum.

the epithelial coat was disorganised, and in the majority it appeared to be almost entirely absent. In many instances not only was this the case, but the sub-epithelial tissues were manifestly affected to a serious extent. The solitary glands were either present in very small numbers only, or could not be recognised at all, and Peyer's patches, in place of presenting their normal aspect, appeared as mere empty networks composed of collections of minute depressions surrounded by slightly elevated ridges. This condition of the patches was very characteristic, and could not be ascribed to causes accidental to the disease, for it appeared as conspicuously in the young children as in the adults or aged people. But the evidences of loss of substance did not end here, for in most cases over considerable areas of the gut, and in some almost universally, the adenoid tissue appeared to be virtually absent. The surface here was quite smooth, the prominences of the villi being almost or entirely unrecognisable, and the muscular coat covered only by a thin membranous investment, seemed to form the inner lining of the tube. Surfaces of this nature corresponded with the transparent, slate-coloured areas visible from the exterior of the intestine. This condition was most pronounced over the lower half or two-thirds of the ileum, but in some cases did not extend quite to the ileo-cæcal opening, a small surface intervening where the process did not seem to have progressed so far, and where the mucous membrane was still distinctly recognisable, although in a more or less disorganised and seemingly disintegrating state. In this site too a certain amount of relative congestion was sometimes present.

Results of microscopic examinations of the tissues of the mucous membrane.

Microscopical examination of the mucous membrane shewed that the epithelium, where present, contained a large amount of fat, the cells including large quantities of oil granules. In the neighbourhood of denuded areas only abortive vestiges of cells and free granular matter were present. In places where the epithelium was absent, the sub-epithelial tissue shewed more or less distinct evidence of similar changes, the nuclei being affected in varying proportions, appearing granular, and in some cases full of distinct oil granules. This condition of the nuclei may have, to some extent, caused the appearance of pigmentation previously described; but in those cases in which the latter was strongly marked a certain proportion of true pigment granules was associated with the oily materials.

Pigmentation of the intestinal ucous membrane not uncommon cases of wasting disease.

It is impossible to decide whether this deposit of pigment in the mucous membrane is essentially connected with the morbid processes giving rise to the symptoms of disease in these cases. The phenomenon is not an uncommon one in cases of long-continued wasting disease, and is generally ascribed o the antecedent occurrence of minute extravasations of blood; but in the human ubject, in these and in the present cases, the deposit may be due to processes imilar to those causing it in the starved amphibian larvæ of the experiments. It may be due to destructive processes in the blood elements generally, rather than to local hæmorrhages and subsequent transformations, the intestinal tissues being merely the special sites of deposit, not the special sites of production of the pigment. In the more advanced stages of atrophy of the mucous membrane the nuclear elements in the villi appeared to be almost entirely absent, and the villi were represented by mere abortive processes containing collections of granular matter.

Phenomena presented by the mucous membrane of the large intestine.

The mucous membrane of the large intestine resembled that of the small one in its extreme general anæmia. Over the greater part of the surface it was dead-white, with faint pink mottling here and there, and, as a rule, its texture was very soft. In some cases this extreme anæmia and pulpiness formed the only remarkable features,—there being no thickening, effusion, or any other evidences of inflammatory action. In other cases there was more or less pronounced thickening; and besides the general softening, distinct evidence of local loss of substance over particular areas was sometimes present. These areas, in some instances, presented characters entitling them to be termed ulcers; but in others they seemed to be merely the result of processes of disintegration and atrophy, like those so strongly developed in the mucous membrane of the small intestine. In such instances there was no evidence of congestion, and the colic lymphatic glands were pale and inconspicuous. The appearances presented by the mucous membrane were sometimes, however, more of the nature of those ordinarily presented in cases of dysentery. In one case this was very decidedly so. In it there was great thickening of the gut, the mucous membrane was broken up into hard rough masses of purple and green colour, distinct ulceration had occurred, there was considerable general congestion, and the lymphatic glands were turgid and of a deep purple colour.

Cases of so-called famine-dysentery really independent of true dysenteric processes.

Taking all the phenomena into account, these cases certainly shew that fatal cases of so-called "famine-dysentery" may occur, in which no true dysenteric processes, as ordinarily understood, are present. The essential process appears to be of the same nature as that affecting the small intestines, but it may be complicated in various degrees by the supervention of true dysenteric changes.

Characters of the liver.

The liver was small. In only one case did it reach the margin of the ribs; in all the others it lay well up beneath the ribs; and the only portion visible on first opening the abdominal cavity was a small surface in the epigastric triangle. In almost every case it was very pale externally and on section was yellowish and fatty looking. In two cases it was of normal colour and general appearance, and in these the microscopic characters of the hepatic tissue were healthy. In the other cases many of the cells were full of fatty granules, and in two this condition was extremely pronounced. The gall-bladder in all cases was half full of bile; in those in which the liver otherwise appeared healthy the fluid presented the characters of normal bile; in all the others it was pale yellow, and in some it was also of a peculiar thick consistence. The limited number of the cases renders it impossible to determine whether the fatty condition present in most of the livers were essentially connected with the antecedent starvation, and an evidence of the preliminary stage of a condition analogous to that observed in the experiments on starvation.

Extreme diminution in bulk of the spleen.

The spleen in every case was of small size and firm texture, and in most instances was conspicuously so, presenting a very remarkable contrast in these respects to the organ as usually observed in India. In some cases the diminution in bulk was exceptionally great, and the organ seemed to consist of little save a dense contracted mass of stroma enveloped in a bluish white shrivelled capsule.

Condition of the kidneys.

The kidneys, like the other organs and tissues, were, as a rule, very pale and anæmic, both externally and on section. In several cases the epithelium was distinctly fatty, the cells being loaded with oil-granules. The consistence varied considerably; in some it was firm, in others very soft. In cases I and II, where the subjects were people in advanced life, the cortical substance was present only in small portion, and the surface was rather granular. Here, again, the number of cases prevents the decision of the question, whether the fatty condition s merely accidental, or dependent on mal-nutrition. The phenomenon is, how-er, worthy of mention in connection with the fact that œdema is one of the mptoms frequently observed in advanced stages of starvation. This may, of urse, be ascribed to general conditions, but it may also possibly owe its origin changes in the renal tissues.

The pancreas.

The pancreas in some cases was normal in appearance; in others the substance seemed as though it were opened out,—the lobules being widely separate, and affording a beauti-l demonstration of the structure of the gland.

The brain unaffected.

The brain presented little calling for special note. In three cases it appeared slightly anæmic, and in four, including the three former, its consistence was somewhat soft. In the her cases the consistence and blood-supply appeared quite normal. In every se, save one, the dura mater was almost everywhere densely adherent to the anium, rendering the removal of the brain a matter of some difficulty.

Microscopical characters of the ood.

In addition to the *post mortem* examinations of the tissues and organs in ses of famine-diarrhœa and dysentery, and as a supplement to them, a cer-in number of examinations of blood were made, the specimens being obtained from cases of the diseases during life, and from inmates of the relief camp of the class likely to ass on into such conditions. The blood was received direct on the glass slides n which it was to be examined, and was at once treated with vapour of osmic cid, so as to fix it unaltered for future detailed examination. When micro-copically examined the specimens presented little which could be regarded as n any respect specially characteristic. The red corpuscles were of normal as-ect, and the proportions of them present in the thin films of blood employed in he preparations did not appear to differ from those present in similarly pre-pared specimens obtained from healthy subjects. Taking this into account long with the great diminution in the bulk of blood so conspicuously manifest-ed by the tissues and organs after death, it would appear that there is a general decrease in both the solid and liquid constituents of the fluid, and not a relative anæmia only. Almost all the specimens were characterised by the very small number of white corpuscles present in them—a phenomenon which appears fairly ascribable to the antecedent conditions of defective nutrition.

General results of the autopsies.

The general result of the entire series of observations was to shew that the disease-conditions under investigation were specially characterised by extreme general anæmia and destructive processes affecting the mucous membrane of the intestinal canal.

CHAPTER IV.

CONCLUSION.

such cases of diarrhœa and
ntery essentially diseases of
ation?

have now to consider what the phenomena just described indicate in
regard to the essential nature and origin of the
disease-processes proximately causing death. The
prominent symptoms observed during life are those
liarrhœa and dysentery; we must attempt to ascertain whether and how far
diseases merit the titles of "famine-diarrhœa" and "famine-dysentery." Any
ns of disease occurring during periods of famine may, in a sense, be termed
ıine-diseases; conditions of scarcity and distress must, no doubt, more or
favour the prevalence of all diseases. Cholera and smallpox, for example,
bably find in the famine-stricken a most favourable field, but there is no
lence to prove that famine alone can produce either the one or the other.
other words these and other diseases are not directly due to famine, but
y may and probably do become much more prevalent in consequence of
ıine than they otherwise would have been. But is there evidence to
w that the so-called "famine-diarrhœa" and "famine-dysentery" possess
racters, either in their symptoms or in their pathological appearances, suffi-
ıt to distinguish them as the results of insufficient nutrition? Does the
lence regarding them justify us in believing that special forms of intestinal
ase prevail during periods of scarcity, essentially dependent on the effects
insufficient nutritive supply? It appears to me that it does. Subjects of
ıine are of course exposed to the ordinary exciting causes of diarrhœa and
entery, and may probably be specially susceptible to their influence; but
pathological phenomena characterising many cases of such disease in them
ear to indicate very distinctly that the predisposing cause is starvation, and
t the symptoms are fundamentally due to destructive changes in the mucous
mbrane of the digestive canal induced by imperfect nutrition.

sults of starvation in the tis-
of the human subject analo-
to those obtained by experi-
t.

On comparing the results of the autopsies in cases of these diseases with
those obtained by experiment, it appears clear that
the changes effected by defective nutritive-supply
in the human subject are closely analogous to those

occurring in the amphibian larvæ. In both cases a fatty change and subsequent disappearance of tissue elements occurs; and in both this change is specially pronounced in the tissues of the intestinal apparatus. The phenomena observed in the human subject shew as distinctly as those in the amphibian larvæ that the effects of famine on the tissues are to produce an actual destruction of tissue, and not a mere atrophic diminution of bulk as affirmed by Bauer. The great diminution in the mass of the blood, which forms such a conspicuous phenomenon in starvation, would of itself seem to indicate that destruction of tissue elements occurs, unless it be demonstrated that the anæmia is merely relative and solely due to diminution of the fluid constituents of the blood; but the phenomena occurring in the intestinal canal appear to be quite decisive. Without the experimental data it might have remained a more open question whether the conditions in the human subject were not rather secondary phenomena, dependent on the fatal diarrhœa and dysentery, or due to some occult cause inducing the latter; but when taken along with the phenomena of uncomplicated starvation in the larvæ, they appear unequivocally traceable to the influence of defective nutrition. The clinical experience obtained in the conduct of relief-camps also affords most conclusive evidence on the question. Had all the tissues retained their integrity and capability of performing their proper functions, the excessive mortality and the general futility of the most careful dietetic treatment among cases of advanced starvation would remain utterly inexplicable.

Destructive change in the intestinal tissues an effective cause for the production of diarrhœa and dysentery.

When, however, we recognise the existence of destructive change in the tissues of the intestinal canal, these problems admit of ready solution, and all occasion to call in arbitrary explanations of the prevalence of fatal diarrhœa and dysentery among the subjects of starvation ceases. It has been usual to ascribe these symptoms to the influence of noxious materials in the blood derived from abnormal transformations of tissue, and such materials may, no doubt, be present, but the local effects produced on the intestinal tissues appear to be quite sufficient to account for the symptoms. It has also been indicated, as a curious effect of starvation, that it should produce an incapacity for the assimilation of food when supplied.[1] With the present anatomical data vould rather be a matter of wonder if it did not. With the degenera- and destruction of the epithelial and glandular elements of the mucous nbrane of the digestive system, the digestion and assimilation of nutritive erials supplied in the food must necessarily be impaired or destroyed, accord- to the degree of morbid change. The food-elements, not being submitted to ir normal transformations, become mere foreign bodies liable to undergo omposition, and well adapted to cause irritation, especially on surfaces which re been more or less denuded of their normal protective coverings, as is the e with the intestinal mucous membrane after the destruction of its epithe- m.

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[1] Carpenter; op. cit., p. 112.

xplanation of frequent onset of symptoms in the relief-camps.

That symptoms of intestinal irritation should set in under such circumstances is only what might be expected, and that these symptoms should have been especially liable occur in people shortly after admission into relief-camps is readily explic- le. While they were outside and actually suffering from extreme priva- on, the primary destruction of tissue was no doubt advancing, but the amount nutritive material ingested was correspondingly reduced, and was so small as be within the control of the remaining digestive tissues. On admission into amp a larger amount of food was supplied; the digestive and absorptive pparatus which had formerly sufficed was now relatively greatly reduced, and he surplus food-elements became mere sources of irritation. It has long been ecognised that great caution is necessary in regard to food-supply after even omparatively slight starvation. Where changes in the tissues have only been light, careful dietetic treatment, so as to avoid irritation, may suffice to tide over the danger, and ultimately effect a cure. Where, however, extensive destruction of the tissue-elements of the mucous membrane has taken place, it is clear that no dietetic treatment, however carefully carried out, can be expected to effect recovery: dietetic treatment may save a weakened mucous membrane; it cannot make a new one.

Necessity of caution in regard to dietetic experiments.

All the phenomena observed in the present series of investigations point to the absolute necessity of great caution in regard to dietetic experiments, dietetic systems of punishment, &c. They shew that it is not safe to push such procedures in the belief that, so long as no evident active evil results present themselves, we can at any time pull up and restore things to their normal state. The fact that in so many cases the fatal diarrhœa and dysentery first manifested itself in people after their admission into the relief-camps is very significant. The people in such cases were admitted into camp, shewing, no doubt, symptoms of extreme general mal-nutrition, but suffering from no active symptoms of disease. The mischief had, however, been irrevocably accomplished, and it only required a change—a favourable change too—in conditions to cause it to manifest itself.

Practical bearing of the character of the changes in the tissues on the question of management of famines.

The insidious character of the mischief has a most important bearing on the practical question of the management of famines. Due to it relief-camps may, to a great extent, be rendered useless by the people failing to have recourse to them, until it is too late. They, too, are likely to be deluded by the idea that, where no active symptoms have appeared, no permanent damage has been done, and that they may safely delay until their distress has counterbalanced their natural inertness and dislike of disturbing their ordinary habits.

Calcutta, October 1878.

ON CERTAIN EFFECTS

OF

STARVATION ON VEGETABLE AND ANIMAL TISSUES.

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